# JORDAN AND HAMBURG LLP 30 OCT 2000

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09/674370

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Docket No. F-6689 Date October 30, 2000

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Washington, D. C. 20231  [ ] ATTN: BOX PATENT APPLIC [ X ] ATTN: BOX PCT  [ X ] ATTN: BOX PCT  [ X ] ATTN: BOX PCT  [ April 29, 1999	ATION
Sir:	
transmitted herewith for filing is the [X] Utility [] Design patent application of:	
inventor/Application Identifier: Kristina SCHMIDT et al.	
Fer: DEVICE FOR TRANSPORTING LIQUIDS ALONG PREDETERMINED GUIDEW	AYS
Enclosed are:	
	he
CLAIMS FILED	
For Number Filed Number Extra Rate Basic Fee \$	
Independent Claims         1         (over 3)         x \$80.00           [ X ] Multiple Dependent Claim         \$270.00         \$2	70.00 63.00
[ ] Foreign Language Filing Fee \$130.00	
[X] Please charge Deposit Account No. 10-1250 in the amount of	3.00
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37 CFR 1.16; 37 CFR 1.17; 37 CFR 1.492.

## 09/674370

534 Rec'd PCT/PTC 3 0 OCT 2000

C. Bruce Hamburg Reg. No. 22,389 Attorney for Applicants

[X]	Return Receipt Postcard 30 UCT 2
[ <b>X</b> ]	Preliminary Amendment
[ <b>X</b> ]	Assignment to Graffinity Pharmaceutical Design GmbH .
	<ul> <li>[ ] Assignment is of record in prior application Serial No</li> <li>[ X ] Assignment Recordation Form Cover Sheet.</li> <li>[ X ] Charge \$40.00 to Deposit Account No. 10-1250 for recording Assignment.</li> </ul>
[ ]	Information Disclosure Statement and/or Information Disclosure Citation
[ ]	English translation
[X]	Small Entity Status is asserted.
[ ]	Applicant hereby claims the benefit of the filing date of the following provisional application(s) under the provisions of 35 USC 119.
	Applicant hereby claims the benefit of the filing date of the following applications under the provisions of 35 USC 119 of which certified copies [ ] will follow [ ] are enclosed [ X ] have been filed in the International Bureau [ ] were filed in prior application No  German Patent Appln. No. 198 19 302.5 filed April 30, 1998  German Patent Appln. No. 198 27 754.7 filed June 23, 1998.
The state of the s	This is a [ ] Continuation [ ] Divisional [ ] Continuation-in-Part of prior application Serial No
	Amend the specification by inserting before the first line the sentence:This is a [ ] continuation, [ ] division, [ ] continuation-in-part, of application Serial No. , filed
	JORDAN AND HAMBURG LLP
	By St.

2 of 2

F-6689

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Applicant** 

Kristina SCHMIDT et al.

Serial No.

(U.S. National Stage of PCT/EP99/03104

filed April 29, 1999)

Filed

(Concurrently herewith)

For

DEVICE FOR TRANSPORTING LIQUIDS ALONG

PREDETERMINED GUIDEWAYS

Assistant Commissioner for Patents Washington, D.C. 20231

:

### PRELIMINARY AMENDMENT

Sir:

Preliminary to examination, please amend this application as follows:

#### **IN THE CLAIMS:**

1. A device for transporting liquids along predetermined guideways, which are provided in a body [(2)], whereby the structures forming the guideways are [adapted to be] attached to a corresponding complementarily shaped opposite body [(1)], [characterized in that] wherein the body [(2)] is provided with recesses [(21)] and [capillary gap forming] elevations [(22)], which form capillary gaps for transporting liquids exclusively by capillary forces, and [in that] at least one liquid supply means (3) adapted to be dosed is associated with the elevations and means [(5)] for spacing apart are provided, whereby between each adjacent elevations [(22)] there remains such a large recess [(21)], having a width of at least 1,000 µm and a depth of at least

 $1,5000 \mu m$  that [the latter is capillarity inactive] in the range of the recesses a transport of liquids by capillary force is eliminated.

Please cancel claim 2.

- 3. A device as claimed in claim 1, [characterized in that] wherein each capillary gap [(4)] is provided with a discrete liquid supply means [(3)].
- 4. A device as claimed in claim 1, [characterized in that] wherein the body [(2)] supporting the elevations [(22)] and the recesses [(21)] is formed by a plane cover plate [(23)].
- 5. A device as claimed in [claims 1 and] <u>claim</u> 4, [characterized in that] <u>wherein</u> the opposite body [(1)] is formed by a plane support plate [(11)].
- 6. A device as claimed in [claims 1 and] <u>claim</u> 5, [characterized in that] <u>wherein</u> the spacing means [(5)] are components of the support plate [(11)].
- 7. A device as claimed in claim [1 and] 4, characterized in that the spacing means [(5)] are components of the cover plate [(23)].
- 8. A device as claimed in claim 1, characterized in that the spacing means [(5)] are arranged in the form of regularly distributed bars.
- 9. A device as claimed in claim 1, characterized in that the means [(5)] for spacing apart the body [(2)] and the opposite body [(1)] are designed as discrete spacer elements [(51)] sealingly insertable between the body [(2)] and the opposite body [(1)], said spacer elements [(51)] being given a preselectably defined height (x) in dependence on the fluid to be directed along the capillary gap [(4)].
- 10. A device as claimed in claim 1, characterized in that the capillary gap forming elevations [(22)] are designed as [continuous] through bars.

- 11. A device as claimed in claim [1, 4 and] 5, [characterized in that] wherein the cover plate [(23)] is adapted to be attached to the support plate [(11)] detachably and free of tensions in different directions.
- 12. A device as claimed in claim 1, characterized in that, on the body [(2)], a plurality of capillary gaps [(4)] is provided independently from each other and with an inlet and outlet each [(41; 42)].
- 13. A device as claimed in claim 1, characterized in that, on the body [(2)], a plurality of capillary gaps [(4)] is provided, which are partially or entirely connected to each other, and the respective connected capillary gaps [(4)] are provided with an inlet and outlet [(41; 42)].
- 14. A device as claimed in claim [1, 4 and] 5, [characterized in that] wherein the arrangement and the route of the elevations [(22)] are determined by the liquid guideways [(43)] predetermined on the support plate [(11)].

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- 15. [Application of a device for transporting liquids along predetermined guideways as claimed in at least one of the preceding claims, characterized in that] A device as claimed in any one of claims 1, 3-14, wherein plane, planar or substrate plates provided with recesses are used as the support plates [(11)].
- 16. [Application of a device for transporting liquids along predetermined guideways as claimed in at least one of the preceding claims, characterized in that] A device as claimed in any one of claims 1, 3-14, wherein bio-chips are used as the support plates [(11)].
- 17. [Application of a device for transporting liquids along predetermined guideways as claimed in at least one of the preceding claims, characterized in that] A device as claimed in any

one of claims 1, 3-14, wherein micro-titer plates or nano-titer plates are used as the support plates [(11)].

### **REMARKS**

The foregoing substantively conforms the application to an Article 34 amendment filed in the international stage and makes obvious formal changes in view of U.S. practice.

Respectfully submitted,

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CBH/cj

### 534 Rec'd PCT/PTO 30 OCT 2000

### Device for transporting liquids along predetermined guideways

#### **BACKGROUND OF THE INVENTION**

5 The invention relates to a device for transporting liquids along predetermined guideways.

Devices for transporting liquids along predetermined guideways, for example, in the form of ducts or hoses, have been known for centuries.

With the development of the scientific and technological progress these devices have been more and more miniaturized in certain fields of application, for example, in the high-pressure fluid chromatography or in pipetting systems.

Pipetting systems adapted for use with liquid samples that are mounted on plane support plates have been used for tenth of years in automated laboratory technical fields. The use of this technology permits a parallel, quick and very efficient handling of the samples. Thereby, the samples are mostly arranged in an array so that the identity of the sample can be connected to an area coordinate and thus a precise position control of the pipetting system is possible. With the progress in dosing technology, the commercially available pipetting systems thereby follow a continuous miniaturization, which is set a physical limit below which a reliable dosing of smallest volumes is not feasible any longer.

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Apart from pipetting systems there are methods known for a simultaneous wetting of different parts of plane support plates with various liquids. These methods make use of tightly closed micro-fluid channels, which are formed in that fluid distributing structures are inserted into the support plate and are sealed by a non-structurized cover-

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plate deposited upon the support plate and vice versa, respectively. In WO 97/33737, for example, a structurized cover-plate is disclosed, which is brought into contact to a plane support plate. A cross-over of liquids between the channels is prevented by the tight and non-detachable connection of these plates by, for example, bonding.

The disadvantage of the tight and non-detachably connected systems lies in the fact that the pathways for the liquids are defined rigidly, and any change in distributing the liquids can only be realized by very complex three-dimensional channel guideways and additionally installed valves.

- An example for the three-dimensional channel guideways is disclosed in US-PS 5,681,484, which is used in the clinical diagnostics and the combinatorial-chemical synthesis, whereby multi-layer microstructurized layer constructions of glass and a valve-controlled fluidics are utilized.
- This element of the micro-fluidics has, however, the disadvantage that it cannot be used with plane support plates, but rather requires arrangements of cavities, which are similar to micro-titer plates, for capturing liquids.
- Furthermore and apart from the above described non-detachably connected channel supporting systems out of plane support and cover plate, there are also detachably connected systems. An example for the flexible connection between plane support plate and structurized covering plate is US-PS 5,429,807, in which, by the structure of the cover plate, a plurality of solved DNA synthesis reagents are wetted with chemical reactive groups line-wise on a square glass surface and, in this way, are brought to reaction. Following this reaction, the cover plate in this example is separated from the support plate, rotated by 90°, and again attached to the support so that the support is again wetted in columns with the same set of reagents. In this manner the desired product

combinations are generated at the intersections of columns and lines on the support.

The disadvantage of these detachably connected systems lies in the fact that the support plates and the cover plates made of rigid and non-flexible material can have fine spacings and fissures which, due to the capillary action, are filled so that a non-desired cross-over results between the channels and, thus, a mixing of the different liquids on the support plate.

A detachable joining of the support plate and the cover plate that is free of spacings and thus prevents a cross-over of the liquids requires an inbetween sealing material and an expensive mechanical construction, which renders the system unsuitable for complex reagent distribution series and automations.

#### 15 SUMMARY OF THE INVENTION

It is an object of the present invention to provide a device for transporting liquids along predetermined guideways that avoids a crossover between the different guideways due to capillary action and which obviates the remaining disadvantages of the prior art.

The object is realized by the features of the first claim. Advantageous embodiments are covered by the dependent claims.

The very essence of the invention consists in that the inventional device intentionally generates capillary gaps which accomplish the transport of liquids by the capillary forces, whereby the course of the liquid transport is predetermined by the course of the capillary gaps and a cross-over of the different liquids is eliminated at a mode of operation as specified.

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#### DETAILED DESCRIPTION OF THE INVENTION

In the following, the invention will be explained in more detail by virtue of schematical embodiments. There is shown in:

Fig. 1 a first embodiment of the inventional device;

Fig. 1a a possible liquid input in a device according to Fig. 1;

Fig. 2 a second embodiment of the inventional device.

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In the device for transporting liquids along predetermined guideways, one starts, as shown in Fig. 1, from a body 2, and the structures forming the guideways are adapted to be attached to a respective complementarily shaped opposite body 1. When there is specified within the frame of the invention that the body 2 is complementary shaped relative to the opposite body 1, then this means that, for example, at a plane support plate 11 the body 2 is also plane before the recesses 21 are inserted; analogously this, for example, is true for a convexly shaped body 2 and opposite body 1; or for any other body 2 and opposite body 1 shaped as desired, for example, as tubes. Thereby, the body 2 is provided with elevations 22 forming capillary gaps as well as recesses 21, whereby there remains so large a recess 21, each, between adjacent elevations 22 that the former is capillarily inactive. Furthermore, means 5 for spacing apart are provided in the device, which are shown in Fig. 1 and 2, as well as liquid supply means 3 which permits dosing, as exemplarily shown in Fig. 1a. Thereby at least one liquid supply means 3, which permits dosing, can be associated to the elevations 22.

The forms of the body 2 and the corresponding complementarily shaped opposite body 1 are adapted to be designed as desired, in dependence on the guideways to be formed. So it is possible, however not shown in

detail, that the recesses 21 and the elevations 22 are provided, for example, in a helically tapering shape into the interior wall of a second cylinder engaging a first cylinder, when a guideway is designed, for example, along the longitudinal extension of the surface of a cylinder.

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A particularly advantageous embodiment for special applications, described in the following, of the body 2 supporting the recesses 21 and the elevations 22 is defined, as shown in Fig. 1 and 2, as that of a plane cover plate 23, to which the opposite body 1 is associated in the form of a plane support plate 11

a plane support plate 11.

The spacing means 5 are, as represented in Fig. 1, adapted to be structured as a component of the cover plate 23, respectively as a component of the support plate 11, what is not specially shown, for example, as regularly distributed bars.

Alternatively, as shown in Fig. 2, the spacing means 5 for spacing apart the cover plate 23 and the support plate 11 can be provided as specially designed spacer elements 51 which are sealingly inserted between the cover plate 23 and the support plate 11; the spacer elements 51 are given a definite height x in dependence on the medium, which has to be

20 directed through the capillary gap 4.

The elevations 22 forming the capillary gap are, for example, designed as continuous bars, as shown in Fig. 1 and 2, whereby the arrangement and the route of the elevations 22 correspond to the liquid guideways 43 on the support plate 11. The cover plate 23 is adapted to be attached to the support plate 11 detachably, without tension in different directions. A plurality of capillary gaps 4 is provided, independently from each other on the support plate 1; the capillary gaps 4 being each provided with an inlet and an outlet 41; 42, whereby each capillary gap 4 has a special liquid supply means 3, which is shown in Fig. 1a.

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A plurality of capillary gaps 4 can be provided on the body 2, not shown in detail in the Figures; thereby the capillary gaps 4 can be partially or completely connected to each other and each can have an inlet and outlet 41; 42. Thereby the inventional device is particularly well suited for complex reagent distribution series and automation, for example, on the basis of plane supports.

The dimensions of the capillary gap 4 are, depending on the wettability of the materials used for the body 2 and the opposite body 1 and on the state of the fluids to be guided, determined in that exclusively capillary forces act upon the liquids to be transported. The dimensions for the recesses are such that they themselves are capillarily inactive.

With respect to an application of the inventional devices, the elevations 22, running parallel to each other, have, for example, a width b in an order of size of 1.25 mm, the recesses 21 a width a of at least 1,000 $\mu$ m and a depth of at least 1,500 $\mu$ m. Under consideration of the properties of the materials and liquids, the generated capillary gap 4 has a length in an order of size of 200 mm. The height x of the spacing between the support plate 11 and the cover plate 23 lies, in the example, in an order of size of from  $1\mu$ m to  $1,000\mu$ m.

For generating the recesses 21 and the elevations 22, which can be arranged as desired (for example, in parallel, branching out, or meandered) structuring technologies, for example, are used as they are known from the semiconductor production (for example, etching techniques or laser ablation), wherein, for example, borofloat-glass, which has a high flatness of the surface, is used as a material for the cover plates 23.

A further possibility of providing the recesses 21 into the cover plate 23 lies, for example, in the use of diamond tools.

Another way to realize a cover plate 23 having parallel recesses 21 and elevations 22 consists in that stripes, for example, out of material selectable as desired and having different dimensions are so connected with each other (for example, by bonding or melting) that an arrangement of recesses 21 and elevations 22, for example, in analogy to Fig. 1 is obtained.

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The spacing means 5 are connected, for example, by bonding or melting to the cover plate 23 and the support plate 11, respectively, or they are laid in loosely between the plates 11 and 23. Alternatively, the spacing means 5 can be directly worked out of the material of the support plate 11 or the cover plate 23 by the structurizing technologies used.

The different liquids, when using the inventional device, are transported by the liquid supply means 3, shown in Fig. 1a, to the respective inlet 41 of the elevations 22, whereby due to the effective capillary forces the respective capillary gap 4 is filled. The liquid supply is then accomplished either through the liquid supply means 3, shown in the left part of the Fig. 1a, via the cover plate 23 or, where appropriate, through the liquid supply means 3, shown in the right part of the Fig. 1a, that can be provided in the support plate 11. The discharge of the liquid is accomplished via the outlet 42.

For example, plane, planar or substrate plates provided with recesses are used as support plates 11, whereby these recesses can be, for example, cavities provided with micro-beads.

Advantageously, micro-titer plates or nano-titer plates as well as biochips in the form of plane, planar substance libraries can, for example, be used as support plates 11.

In an application of the inventional device, for example, a square support plate 11 of n lines can be wetted with n different liquids by a square

cover plate 23 provided with n+1 recesses 21 which are parallel to each other. After removal of the cover plate 23, the removal of the liquids from the support plate 11, the turning of the cover plate 23 about 90° and establishing again the spaced apart connection between the cover plate 23 and the support plate 11, the wetting with n-columns of n different liquids is feasible, so that an n-n pattern of the intersections of lines and columns results. Due to the application of the device described in the example, an orthogonal liquid distribution as, for example, required in the combinatorial chemistry for the synthesis of substance libraries can be accomplished in a particularly easy manner.

# List of reference numerals

	1	-	opposite body
	2	-	support plate
5	2	-	body
	21	-	recesses
	22	_	elevations
	23	_	cover plate
	3	_	liquid supply means
10	4	_	capillary gap
	41	_	inlet
	42	-	outlet
	43	-	liquid guideways
	44	-	spacing means
15	45	-	spacer elements
	a	-	width of recesses
	b	-	width of elevations
	X	-	height

### **Claims**

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- 1. A device for transporting liquids along predetermined guideways, which are provided in a body (2), whereby the structures forming the guideways are adapted to be attached to a corresponding complementarily shaped opposite body (1), characterized in that the body (2) is provided with recesses (21) and capillary gap forming elevations (22), and in that means (5) for spacing apart are provided, whereby between each adjacent elevations (22) there remains such a large recess (21) that the latter is capillarily inactive.
- 2. A device as claimed in claim 1, characterized in that at least one liquid supply means (3) adapted to be dosed is associated to the elevations (22).
- 3. A device as claimed in claim 1, characterized in that each capillary gap (4) is provided with a discrete liquid supply means (3).
- 4. A device as claimed in claim 1, characterized in that the body (2) supporting the elevations (22) and the recesses (21) is formed by a plane cover plate (23).
  - 5. A device as claimed in claims 1 and 4, characterized in that the opposite body (1) is formed by a plane support plate (11).
  - 6. A device as claimed in claims 1 and 5, characterized in that the spacing means (5) are components of the support plate (11).
- 7. A device as claimed in claim 1 and 4, characterized in that the spacing means (5) are components of the cover plate (23).

- 8. A device as claimed in claim 1, characterized in that the spacing means (5) are arranged in the form of regularly distributed bars.
- 9. A device as claimed in claim 1, characterized in that the means (5) for spacing apart the body (2) and the opposite body (1) are designed as discrete spacer elements (51) sealingly insertable between the body (2) and the opposite body (1), said spacer elements (51) being given a preselectably defined height (x) in dependence on the fluid to be directed along the capillary gap (4).
  - 10. A device as claimed in claim 1, characterized in that the capillary gap forming elevations (22) are designed as continuous bars.
- 15 11. A device as claimed in claim 1, 4 and 5, characterized in that the cover plate (23) is adapted to be attached to the support plate (11) detachably and free of tensions in different directions.
- 12. A device as claimed in claim 1, characterized in that, on the body (2), a plurality of capillary gaps (4) is provided independently from each other and with an inlet and outlet each (41; 42).
- 13. A device as claimed in claim 1, characterized in that, on the body (2), a plurality of capillary gaps (4) is provided, which are partially or entirely connected to each other, and the respective connected capillary gaps (4) are provided with an inlet and outlet (41; 42).
  - 14. A device as claimed in claim 1, 4 and 5, characterized in that the arrangement and the route of the elevations (22) are determined by the liquid guideways (43) predetermined on the support plate (11).

15. Application of a device for transporting liquids along predetermined guideways as claimed in at least one of the preceding claims, characterized in that plane, planar or substrate plates provided with recesses are used as support plates (11).

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- 16. Application of a device for transporting liquids along predetermined guideways as claimed in at least one of the preceding claims, characterized in that bio-chips are used as support plates (11).
- 17. Application of a device for transporting liquids along predetermined guideways as claimed in at least one of the preceding claims, characterized in that micro-titer plates or nano-titer plates are used as support plates (11).

#### Abstract

The invention relates to a device for transporting liquids along predetermined guideways. The aim is to provide a device of this type which prevents the undesirable interaction between different guideways which can otherwise be caused by capillary effects. To this end, the device has guideways which are provided in a body (2). The structures forming the guideways can be placed on a corresponding complementarily shaped counterbody (1). The device is also configured in such a way that the body (2) has raised sections (22) which form a capillary gap, and recesses (21). Spacing elements (5) are also provided and there is always a large enough recess (21) between adjacent raised sections (22) to ensure that said recess has no capillary action.

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# COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

(Includes Reference to PCT International Applications)

Attorney's Docket Number

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

"DEVICE FOR	TD ANGRODEING LIGHTER	ALONG PREDETERMIND GUIDEWAY	7011
DEVICE FUR	. IRANSPURTING LIQUIDS	- ALONG PKEDETEKMIND GUIDEWAY	· 5."

the spec	cifica	ation of which (check only one item below):	
[	]	is attached hereto.	
[	]	was filed as United States application	
		Serial No.	
		on	
		and was amended	
		on	(if applicable).
$\bowtie$	[]	was filed as PCT international application	
		Number PCT/EP99/03104	
		onApril 29., 1999	
		and was amended under PCT Article 19	
		on	(if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

Country (if PCT indicate "PCT")	Application Number	Date of Filing (day, month, year)	Priority Claimed Under 35 USC 119
DE	198 19 302.5	30.04.1998	[X] Yes [ ] No
DE	198 27 754.7	23.06.1998	[≥€Yes []No
			[ ] Yes [ ] No
			[ ] Yes [ ] No
			[ ] Yes [ ] No

Attorney's Docket Number

## COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (Continued)

(Includes Reference to PCT International Applications)

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

	U.S. APPLICATIONS		ST	ATUS (Check C	One)
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